

REMARKS

Claims 32, 37, and 42 have been amended for greater clarity. Support for the claim amendments can be found throughout the specification and original claims. Specifically, support for the recitation of “recognition site” is found, for example, on page 15, lines 20-24. No new matter has been introduced.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Rejections of Claim 32-35, 37-46, and 48-51 under 35 U.S.C. § 112, First Paragraph

Claims 32-35, 37-46, and 48-51 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that is allegedly not adequately described in the disclosure in a way that conveys to one skilled in the art that the applicant possessed the claimed invention at the time the application was filed. Applicants respectfully traverse this rejection.

Specifically, the Examiner asserts that “Applicants claim recombinant vectors of any origin (*e.g.*, viral, plasmid, etc.) that can infect host cells of any type (*e.g.*, human, bacterial, yeast, etc.) via any mechanism (*e.g.*, replicate, integrate, etc.) using any snRNA (U1, U2, U3 ... etc.) using any restriction enzyme . . . one example is not representative of the infinite number of vectors that are currently claimed because the claims encompass a wide variety of different species (*e.g.*, different origin, mechanism, host cell type).” See Office Action, the paragraph bridging pages 3 and 4.

Applicants submit that where, as in this case, (1) the inventive portion of the subject matter is disclosed and (2) any additional variability within the genus arises due to additional elements that are not part of the inventor’s contribution, and when the level of knowledge and skill in the art would allow one skilled in the art to recognize that the applicant was in possession of the genus, the written description cannot be deemed defective. See Written Description Guidelines Training Materials available at, <http://www.uspto.gov/web/offices/pac/writtendesc.pdf> (released March 1, 2000, Example 8, page 35).

Applicants reiterate the arguments of record and contend that the claimed subject matter is described sufficiently in the specification to indicate that Applicants were in

possession of the invention at the time of filing. For example, Applicants direct the Examiner's attention to page 10, line 9 – page 17, line 3, which clearly supports the presently claimed invention. The Written Description Guidelines for the Examination of Patent Applications state that “whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors.” The factors which should be considered include “level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.” Written Description Guidelines for the Examination of Patent Applications, section II, page 1106, column 2 (see also MPEP 2163).

Applicants submit that the specification satisfies the above guidelines. The specification provides a detailed description of the features of the claimed vector. For example, the specification describes that “[t]he language ‘vector’ is intended to include any molecule which can transport genetic material into an organism while retaining the ability to replicate” (see, *e.g.*, page 10, lines 10-12); “[t]he language ‘snRNA’ is intended to include any small nuclear ribonucleic acid. Preferred snRNAs of the invention are those designated as U snRNAs, *e.g.*, U1, U2, U3, U4, U5, U6, U7, U8, U9, U10, U11 or U12” (see, *e.g.*, page 12, lines 17-19); “[t]he isolated DNA contained in the vector can be contacted with a restriction enzyme. Preferred restriction enzymes of the invention are ‘dual cleavage’ restriction enzymes” (see, *e.g.*, page 15, lines 13-15). In addition, the specification provides working examples illustrating the vectors.

Applicants respectfully submit that the Examiner incorrectly asserts that the claimed vector uses any restriction enzyme. Applicants respectfully disagree. For example, claim 32 recites that digestion with a single restriction enzyme excises a restriction fragment which includes said recognition site and forms insertion sites in said nucleotide sequence. Similarly, claim 42 recites that two insertion sites are formed by digestion with a single restriction enzyme to excise a restriction fragment that contains a recognition site for said restriction enzyme. Accordingly, the number of claimed nucleic acid sequences as amended is not overly large because the restriction enzyme belongs to a unique family of restriction endonucleases that excise a fragment containing the recognition site.

Further, at the time this application was filed, snRNAs and vectors for encoding nucleotide sequences such as snRNAs were known and understood. In accordance with the written description guidelines and the MPEP, “[i]nformation which is well known in the art need not be described in detail in the specification.” Written Description Guidelines for the Examination of Patent Applications, section II, page 1105, column 3; MPEP 2163.

The Examiner also asserts that it is not clear what the metes and bounds of “restriction site” are because the claims disclose only a “restriction” site, not a “recognition” site (see Office Action, page 5, lines 14-17).

Solely for greater clarity, independent claims 32 and 42 have been amended to recite a “recognition site” for a restriction enzyme, rather than a “restriction site.” Applicants submit that the term “recognition site” in the context of restriction enzymes is art-recognized. The specification also teaches that “[t]he language ‘recognition site’ is intended to include a short sequence recognized by a particular restriction enzyme or restriction endonuclease.” See, *e.g.*, page 15, lines 23-24.

For the above reasons, Applicants maintain that all pending claims are supported by the specification with sufficient detail, and in light of the detailed description provided in the specification and the high level of skill in the art of molecular biology, that Applicants were in possession of the claimed invention at the time this application was filed. Accordingly, reconsideration and withdrawal of rejection are respectfully requested.

Rejections of Claims 32-34, 41-42, 44-46, 48, and 51 under 35 U.S.C. § 102(b)

Claims 32-34, 41-42, 44-46, 48, and 51 are rejected under 35 U.S.C. § 102(b) over Noonberg *et al.* (WO 95/10607). Applicants respectfully traverse this rejection.

Specifically, the Examiner asserts that Noonberg *et al.* disclose a recombinant vector comprising an isolated nucleotide sequence encoding a U6 snRNA, wherein the U6 snRNA vector has been modified to contain a SmaI site, “such that digestion with a single restriction enzyme excises a restriction fragment which includes a restriction site for said restriction enzyme [i.e., the blunt ends of SmaI cleavage site]” (see Office Action, page 7, lines 6-14).

The Examiner also asserts that it is impossible to determine the metes and bounds of “restriction site” in claims 32 and 42 (see Office Action, page 7, lines 15-16).

As described above, Applicants have amended claims 32, 37, and 42 to recite a “recognition site”, rather than a “restriction site.” The term “recognition site” in the context of restriction enzymes is art-recognized and clear to one of skill in the art.

Applicants reiterate the arguments of record and contend that the pending claims are not anticipated by Noonberg *et al.* Noonberg *et al.* disclose a vector comprising a SmaI recognition site, and digestion of the vector with the SmaI restriction enzyme (see, *e.g.*, page 50, lines 28-29). However, the excised restriction fragment from the digestion does not contain the recognition site for the restriction enzyme SmaI because the restriction enzyme is known to cut within its recognition site (CCC¹GGG). The excised restriction fragment of Noonberg *et al.* does not include a recognition site for the SmaI restriction enzyme (*i.e.*, CCCGGG); it merely contains the blunt ends after SmaI cleavage (*i.e.*, CCC or GGG). Thus, Noonberg *et al.* fail to teach the invention as recited in claims 32 and 42.

For the above reasons, Applicants submit that independent claims 32 and 42, as well as claims dependent thereon, are novel and not obvious in view of the teachings of Noonberg *et al.* because Noonberg *et al.* do not teach or suggest all the elements of the invention of claims 32 and 42. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejections of Claims 32-35, 41-46, 48, and 51 under 35 U.S.C. § 103(a)

Claims 32-35, 41-46, 48, and 51 are rejected under 35 U.S.C. § 103(a) over Noonberg *et al.* (WO 95/10607) in view of the alleged admission of prior art in the specification, Cohen *et al.* (Proc. Natl. Acad. Sci. 91: 10470-10474, 1994), and Tuschl *et al.* (EMBO 17: 2637-2650, 1998). Applicants respectfully traverse this rejection.

Applicants reiterate the arguments of record and contend that the pending claims are not obvious over the cited references. Applicants have presented the arguments above that Noonberg *et al.* do not teach all the elements of the claimed invention, including, but not limited to, inclusion of the recognition site in the restriction fragment excised from the vectors as recited in amended claims 32 and 42.

None of the other cited references bridge the gap between Noonberg *et al.* and the claimed invention as recited in amended claims 32 and 42. Therefore, Applicants submit that none of these cited references teach or suggest all the claim limitations. Even if combined, the proposed combination still does not teach all the elements of the invention of claim 32 or 42. Further, Applicants respectfully submit that the cited references, taken singly or in combination, do not provide an incentive or motivation to make the combination. Thus, at least two requirements for establishing a *prima facie* case of obviousness have not been satisfied.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 32-35, 41-46, 48, and 51 under 35 U.S.C. 103(a).

Rejections of Claims 32-35, 37-46, and 48-51 under 35 U.S.C. § 103(a)

Claims 32-35, 37-46, and 48-51 are rejected under 35 U.S.C. § 103(a) over Noonberg *et al.* (WO 95/10607) in view of the alleged admission of prior art in the specification, Cohen *et al.* (Proc. Natl. Acad. Sci. 91: 10470-10474, 1994), Tuschl *et al.* (EMBO 17: 2637-2650, 1998), and Sears *et al.* (Nucl Acids Res 24: 3590-3592, 1996). Applicants respectfully traverse this rejection.

The Examiner acknowledges that Noonberg *et al.*, Cohen *et al.*, Tuschl *et al.*, and the alleged admission of prior art in the specification do not explicitly disclose the restriction enzyme BaeI or the recognition site for BaeI. However, the Examiner cites Sears *et al.* to establish a *prima facie* case of obviousness.

Applicants note that although claims 32-35, 37-46, and 48-51 are rejected based on this ground, the reasons provided by the Examiner are directed to dependent claims 39-40 and 49-50 only.

Applicants reiterate the arguments of record and contend that the pending claims are not obvious over the cited references. Although Sears *et al.* disclose identification and characterization of a restriction enzyme, BaeI, which cuts double-stranded DNA on both strands upstream and downstream of its recognition site, Sears *et al.* do not teach or suggest use of the BaeI enzyme or similar enzymes in making the vector encoding an snRNA as

recited in claims 32 or 42. Sears *et al.* at most indicate that the BaeI restriction enzyme and recognition site were available at the time the application was filed. However, none of the cited references, in particular, Noonberg *et al.*, teach any benefit or need to use the BaeI enzyme/site which excises its recognition site. In the absence of any direction in the art that Sears' BaeI enzyme/site should be used for making a vector comprising an snRNA-encoding nucleotide sequence, one of ordinary skill in the art would have had no motivation to modify Noonberg's vector with Sears' BaeI enzyme/site.

Thus, the cited references, taken singly or in combination, do not provide a motivation for one of skill in the art to arrive at the claimed invention. Applicants submit that at least one requirement for establishing a *prima facie* case of obviousness has not been satisfied. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 32-35, 37-46, and 48-51 under 35 U.S.C. 103(a).

Rejections of Claims 32-35, 37-46, and 48-51 under 35 U.S.C. § 112, First Paragraph

Claims 32-35, 37-46, and 48-51 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that is allegedly not adequately described in the disclosure in a way that conveys to one skilled in the art that the applicant possessed the claimed invention at the time the application was filed. Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

Specifically, the Examiner asserts that "the deletion of the word 'single' in claim 32 permits the encoding of more than one snRNA in the vectors . . . the increased breadth of possible modification constitute new matter." Claim 42 is rejected for the same reasons. See Office Action, page 21, lines 8-14.

Applicants contend that the recitation of "encoding an snRNA" in claims 32 and 42 is fully supported by the original claims (*e.g.*, claims 1, 9, 27, and 29-31) and throughout the specification. Applicants note that the recitation of "single snRNA" was added via claim amendment after filing of the application. Thus, deletion of the word "single" in claims 32 and 42 does not constitute new matter. Reconsideration and withdrawal of these rejections are respectfully requested.



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Rejections of Claims 32-35, 37-46, and 48-51 under 35 U.S.C. § 112, Second Paragraph

Claims 32-35, 37-46, and 48-51 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

Specifically, the Examiner asserts that the term “restriction site” is vague and indefinite as it is not clear whether the “restriction site” refers to “recognition site” or the “cleavage site” or some other sequence associated with the restriction enzyme such as a “partial recognition site” or a “partial cleavage site.” See Office Action, the paragraph bridging pages 21 and 22.

Solely to expedite prosecution, Applicants have amended claims 32, 37, and 42 to recite the term “recognition site.” Applicants submit that such amendments do not narrow the scope of the pending claims. Reconsideration and withdrawal of these rejections are respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Please charge any deficiency or credit any overpayment in the fees that may be due in this matter to **Deposit Account No. 18-1945, under Order No. WIBL-P01-523.**

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